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EXAMINER
ORWIG, KEVIN S

ART UNIT	PAPER NUMBER
4161	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,449	ROYERE ET AL.	
	Examiner	Art Unit	
	Kevin S. Orwig	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-54* is/are pending in the application.

4a) Of the above claim(s) *49-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 28-54 are currently pending. Claims 28-48 are the subject of this Office Action. This is the first Office Action on the merits of the claims. Non-elected claims 49-54 are withdrawn from consideration.

Election/Restrictions

Applicant's election of Group I (claims 28-48) in the reply filed on Jul. 28, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's election of "the mixture of saturated C_8-C_{18} fatty acids" and "the pharmaceutical active principle" as elected species is acknowledged. It is noted that this election does not properly comply with the species election requirement, wherein applicant was required to specify a *single* crystallizable lipid and a *single* active principle (page 3, end of paragraph 3). Instead of a single elected species, in each case the species election encompasses multiple compounds. For instance, a *mixture* of fatty acids was elected as the species for the crystallizable lipid and a pharmaceutical active principle was elected as the active principle. A pharmaceutical active principle is not a single active principle, but a description of a broad class of compounds. Nonetheless, the examiner has elected to examine this case using these elected species as the basis of examination.

Claims 49-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Priority

The earliest effective U.S. filing date afforded the instantly claimed invention has been determined to be Sep. 30, 2004, the filing date of PCT application PCT/FR04/02480 to which the instant national stage 371 application claims priority. Acknowledgment is made of applicant's claim to foreign priority under 35 U.S.C. 119(a)-(d). The certified copy of the French application was filed with the USPTO on Apr. 12, 2006.

Claim Objections

Claim 47 is objected to because of the following informalities: the word "the" in line three should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-33 and 36-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jansen *et al.* (U.S. Patent Application Publication No. 2004/0071716; Filed Feb. 20, 2002) (hereinafter Jansen *et al.*) in view of Westesen *et al.* (U.S. Patent No. 6,207,178; Issued Mar. 27, 2001) (hereinafter Westesen *et al.*).

2. Jansen *et al.* disclose water-in-oil-in-water (w/o/w) emulsions comprising adjuvants or therapeutical (i.e. active) agents and stabilizing agents (abstract; paragraph [0044]). These emulsions contain a dispersed water-in-oil (w/o) phase (i.e. a lipid phase) in a continuous aqueous phase (example 3). Jansen *et al.* teach the use of emulsifiers (i.e. stabilizing agents), including PEG-30 dipolyhydroxystearate (i.e. Arlacel P135), which comprises two fatty acid chains and one polyethylene glycol (PEG) chain of 30 polyethylene glycol units (examples 1-6). The dispersed lipid phase droplets in these emulsions are from 1-5 μm (example 3), which is considered monodisperse according to the instant specification (paragraph [0039]). Jansen *et al.* do not teach the use of lipids that are crystallizable as defined in the instant specification.

3. However, Westesen *et al.* disclose suspensions of solid lipid particles, which are oil-in-water emulsions of dispersed lipid phase particles in a continuous water phase (abstract; examples 1-3). The lipid particles (i.e. the lipid phase) taught by Westesen *et al.* form matrices that carry bioactive agents (column 10, lines 20-67). The solid lipid particles are made of fats including di- and tri-glycerides of long chain fatty acids that are solid at room temperature (i.e. crystallizable lipids) (column 5, lines 23-26; column 9, lines 20-29). It is noted that the crystallizable lipids may be tripalmitate, a saturated C_{16} fatty acid derivative.

4. Jansen *et al.* teach that an improvement over the prior art is to provide emulsions that are stable (abstract; paragraphs [0010], [0030], and [0037]), have utility in parenteral administration (paragraphs [0030] and [0049]) and have utility as vaccines (abstract; paragraphs [0001], [0012], and [0040]). Westesen *et al.* teach that their compositions are extremely stable (column 12, lines 18-19; claim 1) and that they are useful as delivery systems for a variety of administration routes including, *inter alia*, parenteral (e.g. intravenous), nasal, and pulmonary administration as well as useful as vaccines (abstract; column 1, line 60 to column 2, line 12; column 5, lines 27-32). It is clear that difficulties in obtaining stable, fluid emulsions for the administration routes discussed above were recognized in the art and addressed by both Jansen *et al.* and Westesen *et al*. In light of these teachings, the skilled artisan would have been motivated to include crystallizable lipids in the composition taught by Jansen *et al.* with the expectation of producing a stable emulsion for the delivery of lipophilic active agents in the oil phase, which would be useful for a variety of administration routes. Thus, it

would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to substitute known crystallizable lipid components as taught by Westesen *et al.* in the emulsions of Jansen *et al.* to prepare a drug delivery system with the expected result of solving the same problem, reading on instant claims 28, 30, 33, 36, and 37.

5. Instant claim 29 recites the composition of claim 28 in which an inner aqueous phase is dispersed in the dispersed lipid phase. In this situation, the composition is a water-in-oil-in-water (w/o/w) emulsion. Jansen *et al.* teach w/o/w emulsions in which an "inner" aqueous phase is dispersed in an oil phase comprising Miglyol 840, which is in turn dispersed in another aqueous phase (example 3), reading on instant claim 29.

6. Westesen *et al.* teach that the lipid phase of their compositions may be approximately 11% by weight relative to the total composition weight (see example 2, where 7.84 g lipid phase is dispersed in water to a total weight of 70 g), which is within the range of 0.01-30% by weight, reading on instant claim 31.

7. Jansen *et al.* teach the use of Arlacel P135 (i.e. the stabilizing agent) at 3% by weight, which is within the range of 0.001-30% by weight, reading on instant claim 32.

8. The aqueous phases of the emulsions taught by Jansen *et al.* contain antigens and phosphate buffered saline (PBS) (i.e. a salt). Since PBS contains sodium chloride, it is considered a cryoprotective agent as defined in the instant specification (paragraph [0046]) (example 3), reading on instant claims 38 and 39.

9. Jansen *et al.* teach that the bioactive agents may be antigens (i.e. proteins) which are present in the inner water phase. Furthermore, the lipid particles taught by

Westesen *et al.* form matrices that carry bioactive agents (column 10, lines 20-67). These bioactive agents may be pharmaceutical active principles (column 10, lines 32-60; column 14, line 58 to column 15, line 27), such as, *inter alia*, antibiotics (i.e. antibacterial agents), beta blockers, and vitamins (column 10, lines 32-60). Westesen *et al.* also teach that the bioactive agents may be angiotensin converting enzyme (ACE) inhibitors (column 10, line 40). Since ACE is an exopeptidase, it is a protease. ACE inhibitors are thus protease inhibitors, reading on instant claims 44-48.

10. Westesen *et al.* teach that their compositions may comprise mixtures of bioactive agents (abstract; column 15, lines 52-53). Thus, these compositions can contain at least two active principles, reading on instant claim 40.

11. In the case of the w/o/w emulsion taught by Jansen *et al.* (example 3) the lipid phase (i.e. the dispersed w/o emulsion) contains a water soluble active principle (the antigen compounds), reading on instant claim 41.

12. Westesen *et al.* teach the use of both water soluble compounds (column 10, lines 26-31) and sparingly water soluble compounds (column 14, lines 54-62) as bioactive agents. Westesen *et al.* also teach that their compositions may comprise mixtures of bioactive agents as described above in paragraph 10. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include both a water soluble active principle and a sparingly water soluble active principle in the lipid phase of the emulsions taught by Jansen *et al.* as needed to produce a drug delivery system to treat multiple conditions or to deliver multiple drugs for the same condition, reading on instant claims 42 and 43.

Claims 28, 34, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jansen *et al.* and Westesen *et al.* as applied to claims 28-33 and 36-48 above in further view of Rabussier (U.S. Patent No. 3,258,326; Issued Jun. 28, 1966) (hereinafter Rabussier).

13. The composition of instant claim 28 is taught by Jansen *et al.* and Westesen *et al.* as applied above in paragraphs 1-4. Neither Jansen *et al.* nor Westesen *et al.* teach the use of a thickener or alginic acid salts.

14. However, the use of alginates as components in emulsions is well-known. For instance, Rabussier discloses formulations comprising stable oil-in-water emulsions (column 2, line 31) and hydrophilic colloids (column 2, lines 25-28) for delivery of active agents (column 2, lines 19-22). The hydrophilic colloids taught by Rabussier may be alginates that are added to the water (i.e. the aqueous phase) to maintain stability of the suspension (column 1, lines 34-42; column 3, lines 63-72; claim 7). Furthermore, Rabussier teaches that the alginate may be used in 0.2% by weight (example 4). Since alginates were known in the art in the instantly claimed weight % range, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include this known component as a stabilizer in the composition taught by of Jansen *et al.* and Westesen *et al.* to prepare a more stable drug delivery system, reading on instant claims 34 and 35.

Conclusion

No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KSO

/Ashwin Mehta/
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